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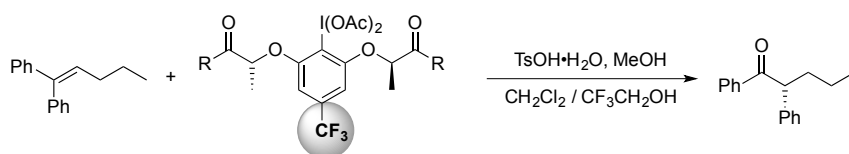


Electron-deficient Chiral Lactic Acid-based Hypervalent Iodine Reagents

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Abstract:

Novel electron-deficient chiral hypervalent iodine reagents were prepared in good overall yields. The reactivity and stereoselectivity of these reagents in oxidative rearrangements of alkenes to α -aryl ketones was investigated. The results show that the new reagents have good reactivity and generate products with high enantiomeric excess.

The chemistry of hypervalent iodine reagents has witnessed a massive growth and development in the 21st century. The extensive interest in hypervalent iodine reagents is attributed to their powerful oxidizing properties, along with their easy handling, commercial availability and benign environmental impact. Their synthetic applications include oxidation, halogenation, amination, C–C bond formation, heterocyclization and rearrangement reactions.^{1,2,3}

Recently, many efforts were devoted to the development of hypervalent iodine catalyzed chemical transformations.⁴ The catalytic cycle relies on the re-oxidation of an iodine(I) species, mainly iodoarenes, into the corresponding hypervalent iodine compounds in the presence of a stoichiometric oxidant. Hydrogen peroxide, oxone, *m*-chloroperbenzoic acid, sodium perborate, and Selectfluor[®] are commonly used terminal oxidants in such catalytic transformations. The utilization of chiral iodoarenes as organocatalysts for different enantioselective transformations is a fast-growing research area and several approaches have been published recently.⁵

Chiral hypervalent iodine(III) reagents have been very successfully used in stereoselective synthesis and received much attention.⁶ Fujita⁷ and Ishihara⁸ initially published the synthesis and use of chiral hypervalent iodine reagents based on lactic acid. Many reactions have been investigated using these chiral reagents and in some of them very high stereoselectivities have been obtained. We also have contributed to that development and published highly stereoselective oxyaminations⁹ and also the first stereoselective rearrangements based on chiral, lactic acid-based iodine(III) reagents.¹⁰ The investigation of more recent rearrangements employing additional orthoesters to generate α -aryl esters as reaction products proved to be less efficient with the known lactic acid-based iodine(III) reagents. We therefore decided to prepare more reactive versions of the reagents **1** by the attachment of an electron-withdrawing group such as a trifluoromethyl substituent ($\text{R} = \text{CF}_3$) in the *para*-position to the iodine (Figure 1). This should enhance the electrophilicity of the hypervalent

iodine reagents **2** ($R = CF_3$) as compared to the unsubstituted reagents **2** ($R = H$). With other hypervalent iodine(III) derivatives we have already shown that the addition of CF_3 groups in *para* position to the iodine(III) moiety enhances their reactivity.¹¹

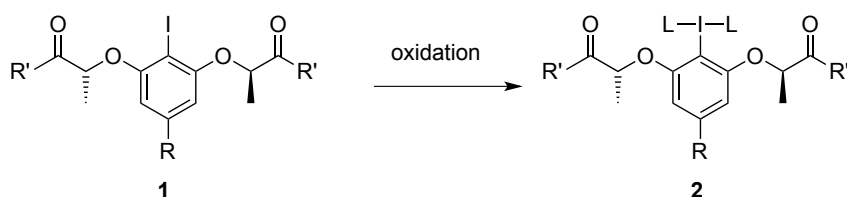
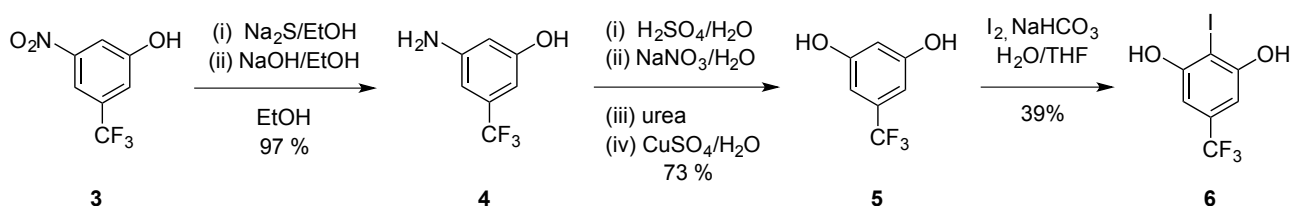


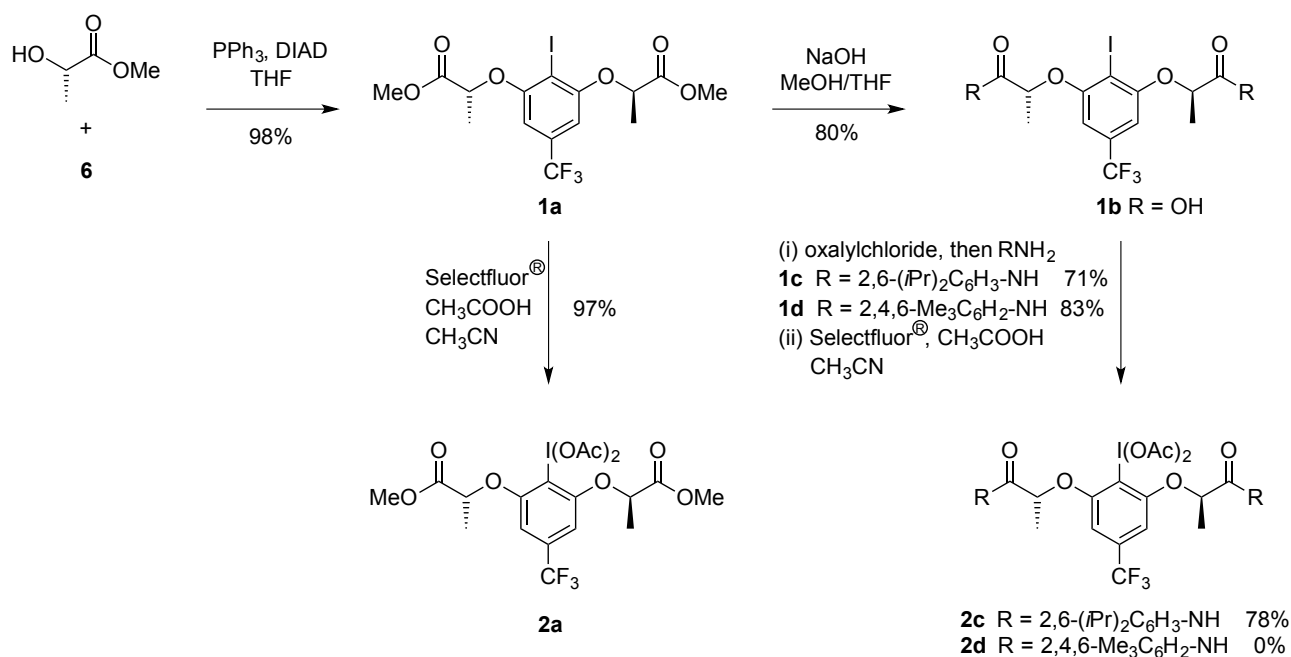
Figure 1: Lactic acid-based hypervalent iodine reagents **2**

Such reagents have been prepared by the route shown below starting from the commercially available 3-nitro-5-(trifluoromethyl)phenol **3** (Scheme 1), through which the novel key building block, 2-iodo-5-(trifluoromethyl)benzene-1,3-diol **6** was accessed. Reduction of the nitro group in **3** to the corresponding amino derivative, 3-amino-5-(trifluoromethyl)phenol **4** was achieved in 97% yield with disodium sulfide in ethanol. Diazotation of **4** was followed by treatment with a saturated aqueous solution of copper sulfate leading to the formation of 5-(trifluoromethyl)benzene-1,3-diol **5** in 73% yield. The desired iodoarene **6** was obtained in 39% yield via the reaction of diol **5** with elemental iodine.¹²



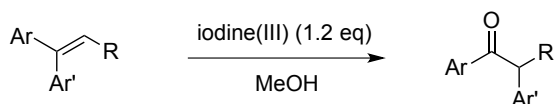
Scheme 1: Synthesis of 2-iodo-5-(trifluoromethyl)benzene-1,3-diol **6**

Having the key intermediate **6** in our hands, we could proceed to achieve the synthesis of the target hypervalent iodine reagents of type **2**. Following literature procedures, the iodoarene **6** was transformed into the lactate based chiral iodoarene derivative **1a** in 98% yield under Mitsunobu reaction conditions. Basic hydrolysis of the diester **1a** afforded the dicarboxylic acid **1b** in 80% yield. Activation of the dicarboxylic acid **1b** followed by the reaction with 2,6-diisopropylaniline and 2,4,6-trimethylaniline afforded the amides **1c** in 71% and **1d** in 83% yield, respectively (Scheme 2). Finally, the chiral iodoarenes were oxidized to the corresponding hypervalent iodine reagents **2a** and **2c** using Selectfluor[®] in a mixture of acetonitrile and acetic acid. The iodine compound **2d** could not be isolated despite many attempts.



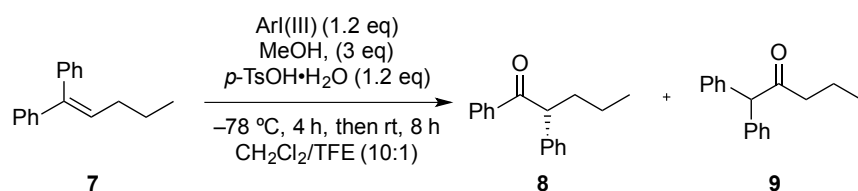
Scheme 2: Synthesis of chiral iodine(III) reagents **2a** and **2c**

Several efficient methods for the synthesis of α -aryl substituted carbonyl compounds through metal-catalyzed cross coupling reactions of ketones are known.¹³ We have reported an efficient metal-free method for synthesizing α -arylated carbonyl compounds *via* an enantioselective oxidative rearrangement of alkenes using stoichiometric chiral hypervalent iodine reagents (Scheme 3).¹⁴ Based on this reaction we have now developed new chiral iodoarenes for accessing α -aryl carbonyl compounds.



Scheme 3: Rearrangement of alkenes to α -arylated ketones

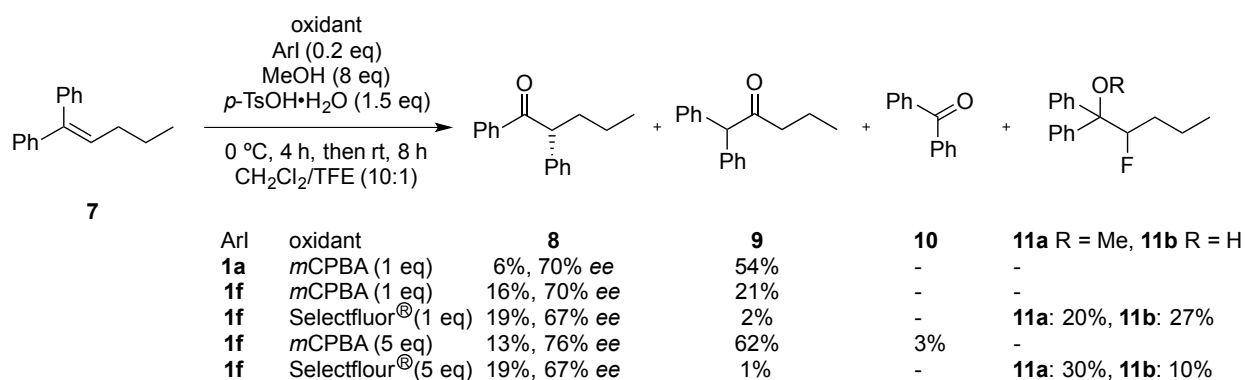
Initially, we explored the oxidative rearrangement of alkene **7** using different chiral iodine(III) reagents as stoichiometric oxidants (1.2 eq). To evaluate the reactivity of the newly prepared hypervalent iodine reagents **2a** and **2c**, we studied the oxidative rearrangement of the alkene **7** by reagents **2a**, **2c** and the previously reported reagents **2e** – **2g** (Table 1).⁸ Reagent **2a** (Table 1, entry 1) with the trifluoromethyl substituent showed comparable reactivity and similar enantioselectivity to the previously reported reagents with either a methyl substituent **2e** or without substituent **2f** (Table 1, entries 2 and 3). Yields range between 45 and 50% while the enantiomeric excess is between 87 and 92%. All reagents produce the same enantiomer of **8** (*R*-configuration), but in each reaction a small amount (5-15%) of ketone **9** is detected as a side product. Reagents **2c** and **2g** with amide functionalities in the side chain showed much lower reactivity (Table 1, entries 4 and 5), while the enantioselectivity is almost identical.



Entry	ArI(III)	8 yield [%]	8 ee [%] (absolute configuration)	9 yield [%]
1	 2a	50	91 (<i>R</i>)	5
2	 2e	45	87 (<i>R</i>)	5
3	 2f	49	92 (<i>R</i>)	10
4	 2c	5	78 (<i>R</i>)	10
5	 2g	15	92 (<i>R</i>)	15

Table 1: Different iodine(III) reagents **2** in the rearrangement of alkene **7**

Furthermore, the potential of the oxidative rearrangement of alkene **7** using different iodoarene catalysts (20 mol%) in presence of a stoichiometric oxidant was investigated. The catalytic reactions had to be performed at a higher reaction temperature as the oxidation to iodine(III) is too slow at low temperature. Initially, several iodoarenes were screened in the presence of one equivalent *m*-chloroperbenzoic acid (*m*CPBA). Substantial amounts of **9** were generated while the overall yield was very low. Enantioselectivities were also low (45-76% *ee*, see supporting information). Different oxidants were also investigated. Although Selectfluor[®] showed reasonable reactivity, fluorinated by-products **11a** and **11b** were always produced by direct reaction with the alkene. Some selected reaction conditions are summarized in Scheme 4.



Scheme 4. Rearrangement with chiral iodoarene catalysts.

Yields of the rearranged reaction product **8** never exceeded 20%, so no catalytic conversion was achieved. Moreover, if the reaction is performed without iodoarene using 1 eq. *m*CPBA, only compound **9** was formed in 71% yield indicating a strong background reaction under the reaction conditions. Further details are found in the supporting information.

In summary, we have synthesized new trifluoromethyl-substituted lactic acid-based hypervalent iodine derivatives, which showed similar behaviour and unfortunately no advantage to the unsubstituted reagents with regards to the stereoselective rearrangement investigated here.

Experimental Section:

All starting materials were purchased from commercial suppliers and used without further purification and all solvents used were dried and purified by standard techniques. Reactions requiring the exclusion of moisture were carried out under an atmosphere of argon or nitrogen in oven-dried glassware. Flash chromatography was carried out using Merck silica gel (35-70 μ m) or on a Biotage Isolera Four platform using SNAP Ultra (25 μ m) cartridges. Melting points were recorded on a Gallenkamp MPD350 apparatus. IR measurements were taken using a Perkin-Elmer 1600 FTIR spectrometer. NMR spectra were recorded on Bruker DPX 300, Bruker DPX 400, or Bruker DPX 500. ¹H NMR spectra were measured at 300, 400 and 500 MHz. ¹³C {¹H} NMR spectra were measured at 75, 100, and 125 MHz using CDCl₃ as the solvent and internal reference. Coupling constants *J* are given in Hz. Multiplicity as follows: s = singlet, d = doublet, t = triplet, q = quartet, sext = sextet, sept = septet, m = multiplet, br = broad. High Resolution Mass Spectrometry (HRMS) was carried out using a Waters LCT Premier XE mass spectrometer using Electrospray Ionisation (ESI). Optical rotations were measured with a UniPol L polarimeter. High-performance liquid chromatography (HPLC) analysis was conducted using Shimadzu LC-10 AD coupled diode array-detector SPD-MA-10A-VP.

3-Amino-5-hydroxybenzotrifluoride **4**¹²

3-Nitro-5-hydroxybenzotrifluoride (5 g, 24.1 mmol) dissolved in ethanol (25 mL) was gently refluxed during the gradual addition of a solution of disodium sulfide (25 g, 104 mmol) in alcohol (100 mL). After 1.5 h, hot 10% ethanolic sodium hydroxide solution (12.5 mL) was added, refluxing continued for 1 hour, then the alcohol removed under reduced pressure. The residue was acidified with hydrochloric acid (2 M) and then neutralised by the addition of sodium hydrogen carbonate solution, and extracted with ether (4 x 50 mL). The combined organic layers were dried

over anhydrous MgSO_4 , filtered, and concentrated under reduced pressure affording 3-amino-5-hydroxybenzotrifluoride **4** as a red solid (4.15 g, 97%).

m.p.: 83 – 85 °C; ^1H NMR (400 MHz, CDCl_3): δ = 6.49 (s, 1H), 6.45 (s, 1H), 6.29 (s, 1H), 4.98 (br s, 1H), 3.84 (s, 2H) ppm.

3,5-Dihydroxybenzotrifluoride **5**¹²

3-Amino-5-hydroxybenzotrifluoride **4** (3.98 g, 22.47 mmol), dissolved in a mixture of water (14 mL) and concentrated sulphuric acid (16 mL). After cooling to 0 °C, a solution of sodium nitrite (1.5 g) in water (8 mL), was added slowly, after 15 minutes, the excess nitrous acid was destroyed by addition of urea. Then the cooled solution was added to a refluxing saturated solution of copper sulfate (200 mL). Then left to cool down to the room temperature and extracted with ether (4 x 50 mL), the combined extracts were dried over anhydrous MgSO_4 , filtered, and concentrated under reduced pressure affording 3,5-dihydroxybenzotrifluoride **5** as a red solid (2.93 g, 73%).

m.p.: 87 – 89 °C; ^1H NMR (400 MHz, CDCl_3): δ = 6.66 (s, 2H), 6.50 (s, 1H), 5.32 (br s, 2H) ppm.

2-Iodo-5-(trifluoromethyl)benzene-1,3-diol **6**¹⁵

3,5-Dihydroxybenzotrifluoride **5** (2.14 g, 12 mmol) was dissolved in $\text{H}_2\text{O}/\text{THF}$ (1:1) (250 mL). After cooling to 0 °C, iodine (3.12 g, 12.6 mmol) was added followed by slow addition of NaHCO_3 (1.108 g, 13.2 mmol). The resulting reaction mixture was stirred for 10 min at 0 °C, then allowed to warm to room temperature and stirred for 40 min. The reaction was then quenched by the addition of a saturated aqueous $\text{Na}_2\text{S}_2\text{O}_3$ solution (10 mL). After extraction with EtOAc (4 x 40 mL), the combined organic phases were dried over anhydrous MgSO_4 and concentrated under reduced pressure. Purification by flash column chromatography (8:2 Hex/EtOAc) afforded the pure product **6** as a yellow solid (1.37 g, 39%).

m.p.: 91 – 92 °C; IR (solid) ν/cm^{-1} : 3277, 1250, 1010; ^1H NMR (300 MHz, CDCl_3): δ = 6.80 (s, 2H), 5.55 (s, 2H) ppm; ^{13}C { ^1H } NMR (126 MHz, CDCl_3): δ = 156.2, 133.2 (q, J = 33.3 Hz), 123.4 (q, J = 272.5 Hz), 104.4, 81.6 ppm; ^{19}F NMR (471 MHz, CDCl_3): δ = –63.32 ppm; HRMS (ESI-TOF) m/z : [M-H] calculated for $\text{C}_7\text{H}_3\text{F}_3\text{IO}_2$ = 302.9130; found: 302.9134.

Dimethyl 2,2'-((2-iodo-5-(trifluoromethyl)-1,3-phenylene)bis(oxy))(2*R*,2'*R*)-dipropionate **1a**¹⁵

2-Iodo-5-(trifluoromethyl)benzene-1,3-diol **6** (1.3 g, 4.27 mmol), was dissolved in dry THF (25 mL) under an argon atmosphere. After addition of methyl (*S*)-lactate (0.897 g, 9.4 mmol), triphenylphosphine (2.6 g, 9.83 mmol) and diisopropyl azodicarboxylate (2 g, 10.26 mmol), the reaction mixture was stirred for 16 h at room temperature and then concentrated under reduced pressure. Purification by flash column chromatography (8:2 Hexane/EtOAc) afforded the pure product **1a** as a colourless solid (1.96 g, 98%).

m.p.: 69 – 71 °C; $[\alpha]_D^{20}$: –90.5° (c = 0.243, CHCl_3); IR (solid) ν/cm^{-1} : 1739, 1244, 1109; ^1H NMR (500 MHz, CDCl_3): δ = 6.58 (s, 2H), 4.83 (q, J = 6.8 Hz, 2H), 3.77 (s, 6H), 1.73 (d, J = 6.8 Hz, 6H) ppm; ^{13}C { ^1H } NMR (126 MHz, CDCl_3): δ = 171.6, 158.7, 132.3 (q, J = 33.6 Hz), 123.6 (q, J = 273.2 Hz), 103.6, 85.3, 74.5, 52.7, 18.6 ppm; ^{19}F NMR (471 MHz, CDCl_3): δ –62.94 ppm; HRMS (ESI-TOF) m/z : [M+Na]⁺ calculated for $\text{C}_{15}\text{H}_{16}\text{F}_3\text{IO}_6\text{Na}$ = 498.9841; found: 498.9847.

(2*R*,2'*R*)-2,2'-((2-iodo-5-(trifluoromethyl)-1,3-phenylene)bis(oxy))dipropionic acid **1b**¹⁵

Dimethyl 2,2'-((2-iodo-5-(trifluoromethyl)-1,3-phenylene)bis(oxy))(2*R*,2'*R*)-dipropionate **1a** (1.683 g, 3.534 mmol) was dissolved in THF/MeOH (1:1) (20 mL). After addition of aqueous NaOH (2 M, 10 mL, 20 mmol, 5.6 eq) the reaction mixture was stirred for 6 h at room temperature and then acidified with aqueous HCl (3 M). After extraction with EtOAc (4 x 40 mL), the combined organic phases were washed with brine, dried over anhydrous MgSO₄ and concentrated under reduced pressure, affording product **1b** as a colourless solid (1.265 g, 80%).

m.p.: 127 – 128 °C; IR (solid) ν/cm^{-1} : 2991, 1705, 1242, 1110; ¹H NMR (500 MHz, DMSO): δ = 13.18 (s, 2H), 6.74 (s, 2H), 5.11 (q, J = 6.7 Hz, 2H), 1.57 (d, J = 6.7 Hz, 6H) ppm; ¹³C {¹H} NMR (126 MHz, CD₃OD): δ = 174.6, 160.3, 132.8 (q, J = 32.8 Hz), 125.2 (q, J = 271.2 Hz), 103.9, 85.4, 75.2, 18.8 ppm; ¹⁹F NMR (471 MHz, DMSO): δ = -61.34 ppm; HRMS (ESI-TOF) m/z : [M-H] calculated for C₁₃H₁₁F₃IO₆ = 446.9553; found: 446.9569.

(2*R*,2'*R*)-2,2'-((2-Iodo-5-(trifluoromethyl)-1,3-phenylene)bis(oxy))bis(*N*-(2,6-diisopropylphenyl)propanamide) **1c¹⁵**

(2*R*,2'*R*)-2,2'-((2-Iodo-5-(trifluoromethyl)-1,3-phenylene)bis(oxy))dipropionic acid **1b** (1.344 g, 3 mmol) was suspended in dry CH₂Cl₂ (30 mL) under an argon atmosphere. After addition of oxalyl chloride (1.33 g, 10.5 mmol, 3.5 eq) and a catalytic amount of DMF the reaction mixture was stirred for 3 h at room temperature and then concentrated in vacuum. The crude product was re-dissolved in dry CH₂Cl₂ (16 mL) under an argon atmosphere and 2,6-diisopropylaniline (2.632 g, 15 mmol, 5 eq) as well as pyridine (0.95 g, 12 mmol) were added. The reaction mixture was stirred for 16 h at room temperature and quenched by the addition of aqueous HCl (3 M). After extraction with CH₂Cl₂, the combined organic phases were dried over anhydrous MgSO₄ and concentrated under reduced pressure. purification by flash column chromatography (8:2 → 2:2 Hex/EtOAc) afforded **1c** as a yellow solid (1.639 g, 71%).

m.p.: 230 – 233 °C; $[\alpha]_D^{20}$: -503 (c = 0.286, CHCl₃); IR (solid) ν/cm^{-1} : 3203, 1660, 1249, 1101; ¹H NMR (300 MHz, CDCl₃): δ = 7.83 (s, 2H), 7.32 (t, J = 7.7 Hz, 2H), 7.18 (d, J = 7.7 Hz, 4H), 6.92 (s, 2H), 5.10 (q, J = 6.6 Hz, 2H), 3.0-2.85 (m, 4H), 1.82 (d, J = 6.5 Hz, 6H), 1.20 (d, J = 6.8 Hz, 12H), 1.15-1.0 (m, 12H) ppm; ¹³C {¹H} NMR (126 MHz, CDCl₃): δ = 169.9, 157.4, 146.1, 133.3 (q, J = 33 Hz), 129.9, 128.9, 123.6, 123.0, 103.6, 84.6, 76.6, 28.8, 22.5, 18.7 ppm; ¹⁹F NMR (471 MHz, CDCl₃): δ = -62.9 ppm; HRMS (ESI-TOF) m/z : [M+H]⁺ calculated for C₃₇H₄₇F₃IN₂O₄ = 767.2527; found: 767.2521.

(2*R*,2'*R*)-2,2'-((2-Iodo-5-(trifluoromethyl)-1,3-phenylene)bis(oxy))bis(*N*-mesitylpropanamide) **1d¹⁵**

(2*R*,2'*R*)-2,2'-((2-Iodo-5-(trifluoromethyl)-1,3-phenylene)bis(oxy))dipropionic acid **1c** (1.286 g, 2.87 mmol) was suspended in dry CH₂Cl₂ (29 mL) under an argon atmosphere. After addition of oxalyl chloride (1.276 g, 10 mmol) and a catalytic amount of DMF the reaction mixture was stirred for 3 h at room temperature and then concentrated in vacuo. The crude product was re-dissolved in dry CH₂Cl₂ (4 mL) under an argon atmosphere and 2,4,6-trimethylaniline (1.54 g, 11.39 mmol, 5 eq) as well as pyridine (0.882 g, 11.16 mmol) were added. The reaction mixture was stirred for 16 h at room temperature and quenched by addition of aqueous HCl (3 M, 10 mL). After extraction with CH₂Cl₂, the combined organic phases were dried over anhydrous MgSO₄ and concentrated under reduced pressure. purification by flash column chromatography (8:2 → 2:2 Hex/EtOAc) afforded pure **1d** as a yellow solid (1.621 g, 83%).

m.p.: 293 – 297 °C; $[\alpha]_D^{20}$: -740 (c = 1.0, CHCl₃); IR (solid) ν/cm^{-1} : 3257, 1670, 1250, 1150; ¹H NMR (300 MHz, CDCl₃): δ = 7.89 (s, 2H), 6.91 (s, 4H), 6.87 (s, 2H), 5.05 (q, J = 6.7 Hz, 2H), 2.27

(s, 6H), 2.16 (s, 12H), 1.82 (d, $J = 6.7$ Hz, 6H) ppm; ^{13}C $\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): $\delta = 168.9$, 157.5, 137.4, 135.1, 129.9, 129.1, 128.8, 122.0, 103.9, 85.0, 76.7, 20.9, 18.8, 18.3 ppm; ^{19}F NMR (471 MHz, CDCl_3): $\delta = -63.00$ ppm; HRMS (ESI-TOF) m/z : $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{31}\text{H}_{35}\text{F}_3\text{IN}_2\text{O}_4 = 683.1588$; found: 683.1594.

Dimethyl 2,2'-((2-(diacetoxy- λ^3 -iodanyl)-5-(trifluoromethyl)-1,3-phenylene)bis(oxy)) (2*R*,2'*R*)-dipropionate 2a⁸

Dimethyl 2,2'-((2-iodo-5-(trifluoromethyl)-1,3-phenylene)bis(oxy))(2*R*,2'*R*)-dipropionate **1a** (0.238 g, 0.5 mmol) and Selectfluor[®] (0.885 g, 2.5 mmol) were dissolved in CH_3CN (16 mL) and glacial acetic acid (5 mL) under N_2 . The reaction mixture was stirred at room temperature overnight. The reaction mixture was concentrated under vacuum then water (25 mL) was added to the residue, and extracted with CH_2Cl_2 (3×20 mL). The combined organic layers were dried over anhydrous MgSO_4 , filtered, and concentrated under reduced pressure, to give **2a** as a yellowish solid (0.288 g, 97%).

m.p.: 195 – 197 °C; $[\alpha]_{\text{D}}^{20}$: -65 ($c = 0.4$, CHCl_3); ^1H NMR (300 MHz, CDCl_3): $\delta = 6.78$ (s, 2H), 4.93 (q, $J = 6.8$ Hz, 2H), 3.77 (s, 6H), 1.98 (s, 6H), 1.70 (d, $J = 6.8$ Hz, 6H); ^{13}C $\{^1\text{H}\}$ NMR (126 MHz, CDCl_3): $\delta = 177.25$, 170.76, 157.08, 137.08 (q, $J = 33.2$ Hz), 122.91 (q, $J = 273.6$ Hz), 110.43, 103.41, 74.90, 52.84, 20.46, 18.35 ppm; ^{19}F NMR (471 MHz, CDCl_3): $\delta = -63.7$ ppm.

(2*R*,2'*R*)-2,2'-((2-(Diacetoxy- λ^3 -iodanyl)-5-(trifluoromethyl)-1,3-phenylene)bis(oxy))bis(N-(2,6-diisopropylphenyl)propanamide) 2c⁸

(2*R*,2'*R*)-2,2'-((2-iodo-5-(trifluoromethyl)-1,3-phenylene)bis(oxy))bis(N-(2,6-diisopropylphenyl)propanamide) **1c** (191.7 mg, 0.25 mmol), Selectfluor[®] (885 mg, 2.5 mmol).

Yield: 78%; m.p.: 220 – 222 °C; $[\alpha]_{\text{D}}^{20}$: -60 ($c = 0.167$, CHCl_3); ^1H NMR (400 MHz, CDCl_3): $\delta = 8.16$ (s, 2H), 7.33–7.2 (m, 2H), 7.18 (s, 2H), 7.11 (s_{br}, 4H), 5.21 (q, $J = 6.7$ Hz, 2H), 2.98 (m, 4H), 1.91 (d, $J = 6.6$ Hz, 6H), 1.44 (s, 6H), 1.3–0.8 (m, 24H) ppm; ^{13}C $\{^1\text{H}\}$ NMR (101 MHz, CDCl_3): $\delta = 176.8$, 169.7, 156.4, 146.1, 129.7, 129.0, 123.6, 103.0, 77.2, 76.9, 28.6, 23.4, 19.5, 19.3 ppm (2 signals (C- CF_3) did not appear in the NMR spectrum). ^{19}F -NMR (471 MHz, CDCl_3): $\delta = -63.05$ ppm.

Compounds **2e**, **2f** and **2g** were prepared following the same procedure as compounds **2a** and **2c**. Their spectral data are in agreement with literature.⁸

Dimethyl 2,2'-((2-(diacetoxy- λ^3 -iodanyl)-5-methyl-1,3-phenylene)bis(oxy))(2*R*,2'*R*)-dipropionate 2e⁸

^1H NMR (400 MHz, CDCl_3): $\delta = 6.37$ (s, 2H), 4.86 (q, $J = 6.8$ Hz, 2H), 3.77 (s, 6H), 2.36 (s, 3H), 1.98 (s, 6H), 1.68 (d, $J = 6.8$ Hz, 6H) ppm.

Dimethyl 2,2'-((2-(diacetoxy- λ^3 -iodanyl)-5-methyl-1,3-phenylene)bis(oxy))(2*R*,2'*R*)-dipropionate 2f⁸

^1H NMR (400 MHz, CDCl_3): $\delta = 7.39$ (t, $J = 8.4$ Hz, 1H), 6.57 (d, $J = 8.4$ Hz, 2H), 4.87 (q, $J = 6.8$ Hz, 2H), 3.75 (s, 6H), 1.98 (s, 6H), 1.68 (d, $J = 6.8$ Hz, 6H) ppm.

(2,6-Bis(((*R*)-1-(mesitylamino)-1-oxopropan-2-yl)oxy)phenyl)- λ^3 -iodanediyl diacetate 2g⁸

¹H NMR (400 MHz, CDCl₃): δ = 8.35 (s, 2H), 7.58 (t, *J* = 8.4 Hz, 1H), 6.93 (d, *J* = 8.4, 2H), 6.8 (s, 4H), 5.15 (q, *J* = 6.6 Hz, 2H), 2.20 (s, 6H), 1.95 – 1.78 (m, 12H), 1.89 (d, *J* = 6.6 Hz, 6H), 1.49 (s, 6H) ppm.

General procedure for catalytic oxidative rearrangement for 1,1-diphenyl-1-pentene by chiral iodine reagents:

To the solution of 1,1-diphenyl-1-pentene (1.0 eq.), iodine reagent (0.2 eq.), *m*CPBA (1.0 eq.), methanol (8.0 eq.) in CH₂Cl₂/TFE (10:1), TsOH•H₂O (1.5 eq.) were added. The reaction mixture was stirred for 4 h at 0 °C then 16 h at room temperature. Quenched with a (1:1) mixture of saturated aqueous NaHCO₃ and saturated aqueous Na₂S₂O₃ (0.5 mL). Then water (4 mL) was added, and the aqueous phase was extracted with CH₂Cl₂ (3 × 5 mL). The combined organic layers were filtered through a TELOS phase separator and concentrated under vacuum to give the crude product. The product 1,2-diphenyl-1-pentanone **8** was isolated by TLC (hexane/ethyl acetate 9:1).

General procedure for the stoichiometric oxidative rearrangement of aryl alkene derivative using chiral hypervalent iodine reagents:¹⁴

To a solution of alkene (0.09 mmol), iodine(III) reagent (0.11 mmol, 1.2 eq) and methanol (0.26 mmol, 3 eq) in CH₂Cl₂:TFE (10:1 v/v) (1.5 mL) at –78 °C, was added TsOH•H₂O (21 mg, 0.11 mmol, 1.2 eq). The reaction was stirred for 4 h at –78 °C, then 16 h at room temperature, then quenched with a 1:1 mixture of aqueous sat. NaHCO₃ and sat. Na₂S₂O₃ (0.5 mL). Water (4 mL) was added and the aqueous phase was extracted with CH₂Cl₂ (3 × 5 mL). The combined organic layers were filtered through a TELOS phase separator and concentrated under vacuum to give the crude product. The product 1,2-diphenyl-1-pentanone **8** was isolated by TLC (hexane/ethyl acetate 9:1).

(2*R*)-1,2-Diphenyl-1-pentanone **8**¹⁴

1,1-Diphenylpentene (20 mg, 0.09 mmol), iodine(III) reagent **1** (65.4 mg, 0.11 mmol), TsOH•H₂O (20 mg, 0.11 mmol) and methanol (11 μL, 0.27 mmol) were reacted according to the general procedure to give the product as a colorless (10 mg, 50%).

¹H NMR (400 MHz, CDCl₃): δ = 7.92 (d, *J* = 7.6 Hz, 2H), 7.44 (t, *J* = 7.4 Hz, 1H), 7.35 (t, *J* = 7.7 Hz, 2H), 7.29 – 7.20 (m, 4H), 7.18–7.12 (m, 1H), 4.52 (t, *J* = 7.3 Hz, 1H), 2.17–2.06 (m, 1H), 1.84 – 1.71 (m, 1H), 1.36 – 1.14 (m, 2H), 0.88 (t, *J* = 7.3 Hz, 3H) ppm.

(2-Fluoro-1-methoxypentane-1,1-diyl)dibenzene **11a**

Colorless oil (48 mg, 30%); IR (neat) ν/cm^{–1}: 3024, 2958, 1076; ¹H NMR (400 MHz, CDCl₃): δ = 7.50 – 6.99 (m, 10H), 5.39 – 5.17 (m, 1H), 3.12 (s, 3H), 1.54 – 1.40 (m, 2H), 1.40 – 1.22 (m, 2H), 0.80 (t, *J* = 7.0 Hz, 3H) ppm; ¹³C {¹H} NMR (126 MHz, CDCl₃): δ = 141.2, 128.6, 127.9, 127.2 (d, *J* = 10.0 Hz), 95.8 (d, *J* = 182.0 Hz), 83.7 (d, *J* = 19.3 Hz), 52.7 (d, *J* = 12.2 Hz), 31.4, 19.1, 13.9 ppm; ¹⁹F NMR (471 MHz, CDCl₃): δ = –186.99 ppm; HRMS (ESI-TOF) *m/z*: [M-MeOH+H]⁺ calculated for C₁₇H₁₈F = 241.1393; found: 241.1393.

2-Fluoro-1,1-diphenylpentan-1-ol **11b**

Colourless solid (15 mg, 10%); m.p.: 109 – 111 °C; IR (solid) ν/cm^{–1}: 3556, 33028, 2958; ¹H NMR (500 MHz, CDCl₃): δ = 7.47 (d, *J* = 7.5 Hz, 2H), 7.35 – 7.10 (m, 8H), 5.31 (dd, *J* = 47.4, 10.2 Hz,

1H), 2.52 (s, 1H), 1.82 – 1.50 (m, 1H), 1.59 – 1.37 (m, 1H), 1.37 – 0.96 (m, 2H), 0.80 (t, $J = 7.1$ Hz, 3H) ppm; ^{13}C { ^1H } NMR (126 MHz, CDCl_3): $\delta = 144.8, 128.3, 127.2$ (d, $J = 20.6$ Hz), 126.8, 125.9, 96.1 (d, $J = 177.8$ Hz), 79.1 (d, $J = 21.0$ Hz), 30.9 (d, $J = 21.2$ Hz), 18.9, 13.8 ppm; ^{19}F NMR (471 MHz, CDCl_3): $\delta = -189.48$ ppm; HRMS (ESI-TOF) m/z : $[\text{M}-\text{H}_2\text{O}+\text{H}]^+$ calculated for $\text{C}_{17}\text{H}_{18}\text{F}$ = 241.1393; found: 241.1390.

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Supporting Information

Catalyst Screening

Oxidant Screening

^1H and ^{13}C NMR spectral data of all compounds

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